IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

IN RE: LIPITOR (ATORVASTATIN CALCIUM) MARKETING, SALES PRACTICES AND PRODUCTS LIABILITY LITIGATION	**MDL No. 2:14-mn-02502-RMG** **This Document Relates to:** *Daniels v. Pfizer Inc.*, No. 2:14-1400 *Hempstead v. Pfizer Inc.*, No. 2:14-1879

DEFENDANT PFIZER INC.'S MOTION TO EXCLUDE THE EXPERT TESTIMONY OF DAVID K. HANDSHOE, M.D., AND MEMORANDUM IN SUPPORT

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Defendant Pfizer Inc. respectfully moves, pursuant to Fed. R. Evid. 104(a), 702, 703, and 403, to exclude the expert testimony of David K. Handshoe, M.D., Plaintiffs' specific causation expert in both *Daniels* and *Hempstead*. Elizabeth Murphy, M.D., is also a specific causation expert in *Hempstead* and is the subject of a separate motion to exclude.

PRELIMINARY STATEMENT

Plaintiffs' general causation experts admit there is no recognized method by which one can reliably determine specific causation: whether Lipitor caused a particular patient's diabetes. None of these experts is aware of any method where you could say in an individual patient by how much Lipitor had an effect on or accelerated their diagnosis of diabetes. Gale Tr. (Ex. 1) at 209:17-210:2. Plaintiffs' expert Dr. Gale, a diabetologist, admits that the question of specific causation is a "difficult issue" for Plaintiffs. *Id.* at 57:18-58:17. Likewise, Dr. Quon, a physician specializing in diabetes, has never told a patient that his or her diabetes was caused by a statin and has never seen a patient who he believes would not have gotten diabetes absent a statin. Quon Tr. (Ex. 2) at 326:18-327:4. Plaintiffs' expert Dr. Singh, a medical doctor, concedes that where "a patient stops taking Lipitor and the diabetes doesn't subside," it "[w]ould be fair to infer that we cannot distinguish whether the diabetes is driven by Lipitor or other factors." Singh Tr. (Ex. 3) at 324:6-325:6. Plaintiffs' expert Dr. Abramson, a former general practice physician, knows of no test or procedure or method to make the determination that Lipitor caused diabetes in individual patients. Abramson Tr. (Ex. 4) at 161:6-25. Plaintiffs' expert Dr. Roberts, a cardiologist, admits there is no methodology that she can use to determine whether a woman who is diagnosed with diabetes would have been diagnosed without taking Lipitor, nor is she aware of any published methodology that would allow a doctor to determine that a woman would not have developed diabetes but for Lipitor. Roberts Tr. (Ex. 5) at 70:12-25. As Dr. Gale explains, attempting to separate out one or two causes in an individual "really resists detailed dissection," Gale Tr. at 79:15-80:4, and it is just not possible to determine whether or not a patient still would have developed diabetes had she not taken Lipitor. *Id.* at 210:14-19.

Rather than designating Dr. Gale or another diabetes expert who treats patients with diabetes to address specific causation, Plaintiffs resort to proffering the opinion testimony of Dr. Handshoe – a pulmonary critical care and sleep medicine specialist who periodically works in the Intensive Care Unit (ICU). Dr. Handshoe claims that his experience with patients in the ICU, some of whom happen to have diabetes, enabled him to create a new diabetes specific causation methodology for purposes of this litigation. He does not purport to rely on the opinions of Plaintiffs' general causation experts, but instead bases his opinion that Lipitor causes diabetes on his own analysis. Dr. Handshoe's dubious expertise warrants a healthy dose of skepticism. His self-created methodology for this litigation is contrary to well-recognized and accepted scientific methods and his opinion should be stricken under *Daubert*.

The two cases before the Court perfectly illustrate why specific causation is such a "difficult issue" for Plaintiffs. Diabetes takes years to develop and the disease process can be present for a decade or more before it progresses to the point of diagnosis. Diabetes also has many well-recognized risk factors, including age, weight gain, metabolic syndrome, family history, and ethnicity. Ms. Daniels and Ms. Hempstead each had multiple well-recognized risk factors that put them well on the road to a diagnosis of diabetes before they ever took Lipitor. For instance, among other things, both were over 40 and overweight or obese when they were diagnosed. Both had a family history of diabetes. Ms. Hempstead's ethnicity is associated with an increased risk of diabetes. Moreover, the magnitude of Plaintiffs' pre-existing risk factors dwarfs the slight increased risk of being diagnosed with diabetes that Plaintiffs claim is associated with statins. None of Plaintiffs' prescribing physicians thinks that Lipitor caused these Plaintiffs' diabetes and all of them think that Lipitor substantially benefitted both Plaintiffs, neither of whom has had an adverse cardiovascular event. Both Plaintiffs took Lipitor for years after their diabetes diagnoses and both continue to take statins to this day.

It falls to Dr. Handshoe to somehow establish that these two high-risk patients for diabetes would not have developed or been diagnosed with diabetes but for their ingestion of Lipitor. Dr. Handshoe claims to have reached his specific causation opinion by conducting a

"differential diagnosis." A differential diagnosis "involves a process of compiling, or ruling in, a comprehensive list of possible causes that are generally capable of causing the illness or disease at issue, and then systematically and scientifically ruling out specific causes until a final, suspected cause remains." *Kilpatrick v. Breg, Inc.*, 613 F.3d 1329, 1342 (11th Cir. 2010). Courts have rejected attempts by experts to establish, by differential diagnosis, that a medication caused a plaintiff's diabetes. *See Guinn v. AstraZeneca Pharm. LP*, 602 F.3d 1245, 1254 (11th Cir. 2010); *Haller v. AstraZeneca Pharm. LP*, 598 F. Supp. 2d 1271, 1303 (M.D. Fla. 2009). Dr. Handshoe's purported differential diagnosis is likewise inadmissible for several reasons.

Dr. Handshoe's reliance on the temporal proximity between Plaintiffs' ingestion of Lipitor and their subsequent diabetes diagnoses is scientifically and legally flawed. Courts have consistently held that offering little more than a temporal relationship between exposure to a substance and the development of a medical condition is insufficient – and, indeed, fallacious – scientific proof of specific causation. As the Eleventh Circuit has held, such reasoning is especially flawed with regard to diabetes, which takes years to develop, thus precluding purported causal inferences based on temporal proximity. *Guinn*, 602 F.3d at 1254.

While Dr. Handshoe claims to have performed a "differential diagnosis," he failed to reliably implement that methodology. To be reliable, a differential diagnosis must reliably and comprehensively "rule in" – and then reliably and scientifically "rule out" – potential alternative causes. *Tamraz v. Lincoln Elec. Co.*, 620 F.3d 665, 674 (6th Cir. 2010); *Kilpatrick*, 613 F.3d at 1342. Dr. Handshoe pays lip service to these steps but he fails to reliably implement them.

Dr. Handshoe failed to rule in many well-recognized risk factors in Ms. Daniels and Ms. Hempstead's medical history. Though an expert's "'fail[ure] to rule out every ***possible*** alternative cause of a plaintiff's illness'" is not necessarily fatal, the failure to "'take serious account of other potential causes'" that are well supported by scientific literature requires exclusion. *Cooper v. Smith & Nephew, Inc.*, 259 F.3d 194, 202 (4th Cir. 2001) (emphasis added) (quoting *Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 265 (4th Cir. 1999)). "Thus, if an expert utterly fails to consider alternative causes … a district court is justified in excluding the

expert's testimony." *Id.* Dr. Handshoe fails to do so, invoking his so-called "clinical judgment" – which is nothing more than his say-so – to sustain opinions that are not supported by science.

A purported differential diagnosis is similarly infirm where the expert fails to rule out alternative causes – that is, if he "fails to offer an explanation for why the proffered alternative cause was not the sole cause." *Id.* Here, Dr. Handshoe admits that he did not rule out any of Plaintiffs' diabetes risk factors. *See* Handshoe *Daniels* Tr. (Ex. 6) at 177:16-178:16; 198:9-17. Instead, he opines that all Plaintiffs' risk factors had an additive effect and that, because they were not diagnosed with diabetes until after taking Lipitor, their diabetes must have been "statin-induced." Dr. Handshoe's admitted failure to seriously consider and scientifically rule out Plaintiffs' preexisting diabetes risk factors renders his purported differential diagnosis unreliable. *See Cooper*, 259 F.3d at 202. Where an expert "has admitted that [plaintiff's] symptoms could have numerous causes," he cannot "simply pick[] the cause that is most advantageous to [plaintiff's] claim." *Viterbo v. Dow Chemical Co.*, 826 F.2d 420, 424 (5th Cir. 1987).

Dr. Handshoe's "reasoning" is the same in both cases with no meaningful differentiation between either Plaintiff. His opinion rests on the fact that each Plaintiff took Lipitor and was then diagnosed with diabetes. That generic opinion would, of course, be the same in every case.

Beyond problems of reliability, Dr. Handshoe's opinions are also inadmissible because they do not fit the facts and issues in this case. At bottom, Dr. Handshoe agrees with Plaintiffs' general causation experts that one cannot determine whether an individual would have developed diabetes without Lipitor. While his Rule 26 report purports to meet the legal standard for causation by claiming that "but for" taking Lipitor, Plaintiffs "would not have developed" diabetes, Handshoe *Daniels* Rpt. (Ex. 7) at 4, at his deposition he testified to the contrary, stating that "[n]obody can say that." Handshoe *Daniels* Tr. (Ex. 6) at 276:12-16. Because he denies the ability to offer an opinion that satisfies the standard for specific causation, his testimony will not "help the trier of fact" and is inadmissible. Fed. R. Evid. 702.

Dr. Handshoe's testimony also changed overnight. One day after admitting there was "no way" for him to determine, among 100 women, who got diabetes from Lipitor, he offered

the "pure speculation" that, among 100 women, "100%" would get diabetes from Lipitor. Such "moving target" made-for-litigation testimony is methodologically unreliable and inadmissible.

Further, despite admitting that in his clinical practice he performs a physical examination when making a differential diagnosis, he performed no such examination here (nor has he ever spoken with Plaintiffs) despite being a Plaintiff's expert with ready access to both Plaintiffs. The Fourth Circuit has affirmed the exclusion of an expert who failed to conduct a physical examination for differential diagnosis in contravention of his professional standards. *Cooper*, 259 F.3d at 203.

Finally, Dr. Handshoe misapplies the Bradford Hill factors, which are designed to assess general causation in population-based studies, not to determine specific causation in an individual. Indeed, he is unclear about what the Bradford Hill factors are and he erroneously asserts that they are the "same methodology" as a differential diagnosis. At his deposition, Dr. Handshoe admitted that he included the Bradford Hill factors in his reports to oblige the lawyers, further underscoring that litigation advocacy, not scientific inquiry, drives his analysis.

FACTUAL BACKGROUND

A. Type 2 Diabetes Is a Multi-Factorial Disease That Takes Years to Develop

"Diabetes is a group of metabolic diseases characterized by hyperglycemia," *i.e.*, elevated blood glucose, that affects the way the body metabolizes sugar, and which results from progressive changes in the body's resistance to, or production of, insulin.[1] The progression from disease initiation to diagnosis is "a long, slow process" that takes "***at least a decade*** or so," Gale Tr. (Ex. 1) at 174:5-175:18; 183:6-12, such that the ultimate diagnosis is "not a new injury" but rather a "milestone" in a progressive disease process. *Id.* at 184:1-8; *accord* Singh Tr. (Ex. 3) at 62:10-25; Abramson Tr. (Ex. 4) at 180:4-182:3. Diabetes is diagnosed by measuring blood glucose levels. There are some 86 million American adults with elevated blood glucose above

[1] ADA, *Diagnosis & Classification of Diabetes Mellitus*, 37 Diabetes Care S81, S81 & S82 (Fig. 1) (2014) (Ex. 8). Under current American Diabetes Association (ADA) diagnostic criteria, a fasting blood sugar level less than 100 mg/dl is normal, 100 to 125 mg/dl is prediabetic, and above 126 mg/dl on two separate tests is diabetic. Fonseca Rpt. (Ex. 9) at 4.

100 mg/dl who have not yet reached the diagnostic threshold of 125 mg/dl and are, thus, deemed to be "prediabetic" since the disease process already has begun.

Plaintiffs' expert, Dr. Gale, concedes that diabetes is a "multifactorial" disease, for which the "causal mechanisms … remain unknown."[2] For this reason, Dr. Gale, a diabetologist, thinks that type 2 diabetes should be referred to as "idiopathic hyperglycemia" – meaning hyperglycemia of unknown causes. Gale Tr. (Ex. 1) at 111:10-19, 113:22-114:9, 144:23-145:8. Dr. Gale states that the four greatest risk factors for diabetes are age, weight, family history, and ethnicity, *id.* at 133:18-23, though age and weight are the "two main drivers." Gale Rpt. (Ex. 10) at 4; *accord* Gale Tr. (Ex. 1) at 134:6-14; Fonseca Rpt. (Ex. 9) at 10; Elasy Rpt. (Ex. 11) at 7; Miller Rpt. (Ex. 13) at 13. Moreover, prediabetes is not just part of the same disease process, it is also a significant risk factor for an eventual diagnosis of diabetes. Gale Rpt. (Ex. 10) at 9-10; Gale Tr. (Ex. 1) at 178:24-180:20.[3] Other recognized risk factors for diabetes include sedentary lifestyle or physical inactivity, hypertension, high triglycerides, low high-density lipoprotein (HDL) cholesterol, metabolic syndrome, depression, psychosis, cigarette smoking, and exposure to some environmental toxins. *See* Handshoe *Daniels* Tr. (Ex. 6) at 116:24-117:5; Quon Tr. (Ex. 2) at 85:10-21; Fonseca Rpt. (Ex. 9) at 6; Elasy Rpt. (Ex. 11) at 7.

Dr. Handshoe asserts that statins such as Lipitor are also risk factors for diabetes and he opines that Lipitor caused these Plaintiffs' diabetes. When asked to quantify that risk, he cites the Waters study[4] – which involved the 80 mg dose of Lipitor, which neither Plaintiff took – to opine that, for a woman with multiple risk factors for diabetes, the relative risk of diabetes attributable to Lipitor is 1.37. Handshoe *Daniels* Tr. (Ex. 6) at 211:11-20; 214:23-215:16.

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[2] Gale, *Is type 2 diabetes a category error?*, 381 Lancet 1956, 1956 (2013) (Ex. 12).

[3] ADA, *Classification & Diagnosis of Diabetes*, 38 Diabetes Care (Supp. 1) S8, at S8-S16 (2015) (Ex. 14).

[4] Waters et al., *Predictors of new-onset diabetes in patients treated with atorvastatin: results from 3 large randomized clinical trials*, 57 J. Am. Coll. Cardiol. 1535, 1535 (2011) (Ex. 15).

Yet as Dr. Gale admits, the very small increase in risk allegedly associated with statins pales in comparison to other large well-recognized risk factors. For example, Dr. Gale admits that obesity is a far greater diabetes risk, Gale Tr. (Ex. 1) at 116:6-16; 178:4-15, and even "night shift work," which disrupts biorhythms, is a stronger risk factor than statins. *Id.* at 176:12-177:6. Pfizer's expert Dr. Hennekens quantitatively addresses the risks of diabetes from weight gain based in part on his research in the landmark Nurses Health Study – which Dr. Handshoe never even heard of. Handshoe *Daniels* Tr. (Ex. 6) at 204:11-21. Started in 1976, the Nurses Health Study is one of "largest and longest running investigations of factors that influence women's health," and has provided "landmark data on cardiovascular disease, diabetes and many other conditions."[5] Dr. Hennekens notes that "[t]he reported magnitude of association between Lipitor and newly diagnosed diabetes, even if real, is small" and is overwhelmed by the large increased risk of diabetes arising from weight gain. Hennekens Rpt. (Ex. 16) at 51.

As Dr. Hennekens explained, the Nurses Health Study shows that even "small increases in body weight from teenage years to adulthood confers alarming risks of type 2 diabetes" such that for "a woman who has gained even a few pounds since age 16, … her risk of developing diabetes due to that weight gain is much greater than what has been postulated about any statin in developing diabetes." Hennekens Tr. (Ex. 17) at 29:22-30:10, 157:2-19. For example, the study shows that, compared to women with a Body Mass Index (BMI) of less than 22, the relative risk of diabetes is 210% for women with a BMI of 22-22.9; 350% with a BMI of 23-23.9; and greater than 500% with a BMI of 25-26.9. Hennekens Rpt. (Ex. 16) at 51-52. To put these BMIs in context, a BMI of 25-29 is considered overweight; obesity begins with a BMI of 30.

Thus, because of the multifactorial nature of the disease, the large magnitude of other risk factors, and the very slight alleged risk of Lipitor, as noted above, none of Plaintiffs' general causation experts is aware of any method where one can say in an individual patient by how much Lipitor had an effect on or accelerated their diagnosis of diabetes. Gale Tr. (Ex. 1) at

[5] The Nurses Health Study, http://www.channing.harvard.edu/nhs/.

209:17-210:2. As Dr. Murphy, another Plaintiffs' specific causation expert in *Hempstead*, concedes, "there's no specific fingerprint or biomarker of Lipitor use," so there is no direct evidence to measure the effect of Lipitor, if any, on the diabetes process. Murphy Tr. (Ex. 18) at 188:14-18; *see also id.* at 152:4-8; 212:14-22, 153:7-153:24. Given the "very complex network of interrelationships within the body ... any attempt at dissection which takes one individual part on its own is going to fall short," Gale Tr. (Ex. 1) at 78:17-79:15, and it is not possible to determine whether a patient still would have developed diabetes had she not taken Lipitor. *Id.* at 210:14-19. This issue is readily apparent from the medical histories of the two Plaintiffs here.

B. Ms. Daniels Had Multiple Pre-Existing Risk Factors for Diabetes

Ms. Daniels is a 67-year old resident of Colorado. *Daniels* Plf. Fact Sheet (Ex. 19) at 1-2; *Daniels* Short Form Compl. (Ex. 20) at 2. She began taking Lipitor in 1997. While the diabetes disease process generally takes at least ten years to progress to the point of diagnosis, in September 1998 she was reporting increased thirst and frequency of urination, Daniels Tr. (Ex. 21) at 220:15-22, which are symptoms of diabetes. She was, depending on the source, prescribed medicine to treat her diabetes in 2000 or 2002. *E.g., id.* at 14:4-22, 208:13-17.

Prior to her diagnosis of diabetes, Ms. Daniels had at least six risk factors for diabetes, which Dr. Handshoe admits are well-recognized. Handshoe *Daniels* Tr. (Ex. 6) at 192:25-196:8, 245:14-24, 112:7-19, 117:13-19. [redacted]

Ms. Daniels also has a family history of diabetes. At least one of her brothers, and her daughter, were diagnosed with Type 2 diabetes, and her paternal grandmother may also have suffered from diabetes. Daniels Tr. (Ex. 21) at 97:19-21, 91:24-92:3, 81:1-6; 89:14-90:21. So, too, among other well-recognized risk factors, she had high triglycerides – 280 mg/dl where the

[6] [redacted] Ms. Daniels's cited medical records are, collectively, Ex. 22.

upper limit of normal is 150 mg/dl. Daniels Tr. (Ex. 21) at 245:14-24. She has had high blood pressure at least since 1997, Handshoe *Daniels* Tr. (Ex. 6) at 118:7-20, [redacted] a genetic condition that causes high cholesterol levels and has a high risk of heart attack, stroke, and death.[10] [redacted] Ms. Daniels had at least five well-recognized CV risk factors: age over 40, [redacted] family history of coronary heart disease (her brother and daughter had heart attacks), metabolic syndrome, and hypertension. Daniels Tr. (Ex. 21) at 159:10-160:1, 78:16-20, 95:19-21, 116:24-117:1; Handshoe *Daniels* Tr. (Ex. 6) at 234:4-235:4; Elasy *Daniels* Rpt. (Ex. 25) at 5.

[redacted] and all of her prescribing physicians confirm that they would still prescribe Lipitor to her today, even if they were given a different warning. Wever 12/14 Tr. (Ex. 26) at 82:12-20; Navarro Tr. (Ex. 27) 78:20-79:2; Pennington 12/14 Tr. (Ex. 28) at 80:21-81:12; [redacted] Despite her high risk profile for a cardiovascular event, she has not experienced one. Daniels Tr. (Ex. 21) at 124:20-125-12, 160:5-21, 164:10-14. [redacted]

[redacted]

[10] Hopkins et al., *Familial Hypercholesterolemias: Prevalence, genetics, diagnosis and screening recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia*, 5 J. Clin. Lipidology S9, S9 (2011) (Ex. 23); Robinson & Goldberg, *Treatment of Adults with Familial Hypercholesterolemia and Evidence for Treatment: Recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia*, 5 J. Clin. Lipidology S18, S18 (2011) (Ex. 24).

[redacted]

[redacted]

None of Ms. Daniels's prescribing physicians opined that Lipitor caused her diabetes. Dr. Day testified that she does "not believe [Lipitor] was a risk factor in her development of diabetes" and believes that Ms. Daniels developed diabetes for reasons unrelated to her use of Lipitor. Day 12/14 Tr. (Ex. 30) at 67:7-68:21. [redacted] Dr. Wever has no opinion whether Lipitor caused Ms. Daniels's diabetes. Wever 12/14 Tr. (Ex. 26) at 85:23-87:17. [redacted]

C. Ms. Hempstead Had Multiple Pre-Existing Risk Factors for Diabetes[16]

Ms. Hempstead is a 71-year-old resident of Texas. *See Hempstead* Second Am. Plf. Fact Sheet (Ex. 33) at 1-2; *Hempstead* Short Form Compl. (Ex. 34) at 2. [redacted] She has not experienced any cardiovascular events, Hempstead Tr. (Ex. 36) at 126:3-12; Charles Hempstead Tr. (Ex. 37) at 138:13-139:4, [redacted]

[redacted]

[16] A more detailed description of Ms. Hempstead's medical history is set forth in Defendants' motion to exclude the testimony of Dr. Murphy, filed contemporaneously herewith. [redacted] Ms. Hempstead's cited medical records are, collectively, Ex. 35.

[redacted]

[redacted] In 2014, after her lawsuit was filed, she continued taking Lipitor and her dose was increased to 40 mg. Hempstead Tr. (Ex. 36) at 156:15-24.

[redacted] She did not begin taking Lipitor until 1999. Ms. Hempstead was diagnosed with diabetes in May 2004, approximately five years after she started taking Lipitor.

Prior to her diagnosis with diabetes, Ms. Hempstead had five of the strongest risk factors for diabetes. She was nearly 60 years old. Hempstead Tr. (Ex. 36) at 186:17-21. Her ethnic heritage is African American and Choctaw, *id.* at 32:11-15, 34:9-11, both of which increase the risk of diabetes.[22] [redacted] Just prior to her diabetes diagnosis, her weight increased to 191 lbs., placing her BMI at 28.6, just below obesity. Handshoe *Hempstead* Rpt. (Ex. 39) at 9. [redacted] Fonseca *Hempstead* Rpt. (Ex. 40) at 4. She also had metabolic syndrome. Handshoe *Hempstead* Tr. (Ex. 36) at 177:8-11. [redacted] Murphy Rpt. (Ex. 43) at 11-15.

None of Ms. Hempstead's treating physicians attributes her diabetes to Lipitor. Dr. Ausmus testified that Ms. Hempstead's diabetes is unrelated to her Lipitor use. Ausmus 1/15 Tr. (Ex. 44) at 84:2-17. Dr. Sabih, her prescribing physician, has never told any patient, including Ms. Hempstead, that taking a statin caused his or her diabetes. Sabih 1/15 Tr. (Ex. 38) at 82:6-9.

[redacted]

[22] *See* ADA, *Classification & Diagnosis of Diabetes* (2015), at S11-12 (Ex. 14); Johnson & Strauss, *Diabetes in Mississippi Choctaw Indians*, 16 Diabetes Care 250 (1993) (Ex. 42).

[redacted]

Ms. Hempstead continues to take Lipitor to this day. Dr. Ausmus stated that Ms. Hempstead has had an "excellent response" and achieved "excellent result[s]" as a result of Lipitor therapy. Ausmus 1/15 Tr. (Ex. 44) at 57:3-23.

ARGUMENT

I. WHO IS DR. HANDSHOE? HE IS NOT AN EXPERT IN DIABETES.

Many physicians regularly treat or study diabetes and have developed an expertise in diabetes. But Dr. Handshoe is not one of them. For instance, Plaintiffs' expert, Dr. Gale, is a diabetologist and former editor-in-chief of *Diabetalogia*. Gale Rpt. (Ex. 10) at 1. Dr. Quon's practice also focuses on studying diabetes. Quon Rpt. (Ex. 45) at 1-2. Despite the ready availability of experts in diabetes, Plaintiffs did not ask Drs. Gale or Quon to opine on specific causation. Perhaps this is because Dr. Gale, like Plaintiffs' other general causation experts, states that it is simply not possible to determine whether a patient still would have developed diabetes had she not taken Lipitor. Gale Tr. (Ex. 1) at 210:14-19. Similarly, Dr. Quon has never told a patient that his or her diabetes was caused by a statin and has never seen a patient who he believes would not have gotten diabetes if they had not taken a statin. Quon Tr. (Ex. 2) at 326:18-327:4. Instead, Plaintiffs sought a specific causation opinion in the first two cases in this MDL from Dr. Handshoe: a pulmonary critical care and sleep medicine specialist.

Dr. Handshoe does not purport to be an expert in diabetes or glucose metabolism. Handshoe *Daniels* Tr. (Ex. 6) at 68:13- 69:3, 70:5-16. He describes his medical practice as "pulmonary critical care and sleep medicine." *Id.* at 50:20-25. He has done no original research relevant to the issues in this case. The only clinical trials he has been involved in concerned drugs used to treat pulmonary conditions and sedation. *Id.* at 43:9-25. He has never conducted any research or investigation of statins outside of this litigation. *Id.* at 44:16-19. Nor has he ever been involved in any research on diabetes outside of this litigation. *Id.* at 45:1-4. Nor has he based his opinions on the reports of Plaintiffs' general causation experts. *Id.* at 33:6-15. Even as an expert witness, he has never previously worked outside the field of pulmonary medicine. *Id.*

at 26:1-4. Rather, his prior litigation work was for workers compensation plaintiffs alleging respiratory injuries. *Id.* at 18:8-20:18, 21:25-22:9.

Dr. Handshoe purports to ground his specific causation opinions in his qualifications in internal medicine, *id.* at 70:17-23, 77:2-6, and periodic treatment of ICU patients, some of whom are diabetic. *Id.* at 49:5-15, 72:18-73:9. Yet he treats hospitalized diabetic patients only while they remain in the ICU and are acutely ill. *Id.* at 54:17-55:11, 57:21-25; Handshoe *Hempstead* Tr. (Ex. 41) at 26:9-20. The only diabetics he sees outside of the ICU are patients who see him for some other condition, but who also happen to have diabetes. Handshoe *Daniels* Tr. (Ex. 6) at 58:7-15. Dr. Handshoe has not seen diabetic patients for regular care in 22 years. *Id.* at 63:18-25, 65:20-25. No physicians refer patients to him for treatment of their diabetes. *Id.* at 62:3-9. He could not think of any reason why patients like Ms. Daniels or Ms. Hempstead would seek medical care from him. *Id.* at 56:5-57:1; *see also* Handshoe *Hempstead* Tr. (Ex. 41) at 26:1-4. Nor is this surprising. Dr. Handshoe's specialties in pulmonary critical care and sleep medicine are far afield from the care and treatment of patients with diabetes. Given his lack of expertise, this Court should view Dr. Handshoe's attempts to reliably show specific causation with a skepticism commensurate with the minimal, if any, expertise he brings to the table.

II. DR. HANDSHOE'S PURPORTED "DIFFERENTIAL DIAGNOSIS" IS UNRELIABLE

Although none of Plaintiffs' general causation experts are aware of a methodology to assess whether a statin caused diabetes in any individual, Dr. Handshoe purports to establish specific causation by applying what he calls a "differential diagnosis" to identify what he calls "statin-induced" diabetes. *See* Handshoe *Daniels* Rpt. (Ex. 7) at 4; Handshoe *Hempstead* Rpt. (Ex. 39) at 4. Dr. Handshoe admits there is no such "clinical entity" as "statin-induced" diabetes, nor are there any diagnostic standards to identify "statin-induced" diabetes. Handshoe *Daniels* Tr. (Ex. 6) at 158:25-160:3. Nor is there any "specific fingerprint or biomarker for Lipitor use," that would operate as direct evidence of its alleged effect in "statin-induced" diabetes. Murphy Tr. (Ex. 18) at 188:6-18. Indeed, Dr. Handshoe admits that Plaintiffs' medical condition and the course of their disease are entirely consistent with non-"statin-induced" diabetes.

Q. Is there anything at all in Mrs. Daniels' medical presentation or her course of disease that is inconsistent with the development and diagnosis of diabetes in a person who never took statins?
A. No.

Handshoe *Daniels* Tr. (Ex. 6) at 162:23-163:3; *see also* Handshoe *Hempstead* Tr. (Ex. 41) at 83:4-11. Rather than a true medical diagnosis, Dr. Handshoe uses the term "statin-induced" diabetes to convey a conclusory assertion regarding causation.

Q. Okay. What does the term mean to you?
A. Well, statin induced diabetes would be a drug induced diabetes.
Q. Are there any other published criteria or diagnostic standards for statin induced diabetes?
A. No.

Handshoe *Daniels* Tr. (Ex. 6) at 159:3-160:3. Dr. Handshoe further admits that patients who supposedly have "statin-induced" diabetes present just like patients with regular diabetes. There are no unique symptoms, clinical features, laboratory values, or diagnostic tests that would enable him or anyone else to determine whether a patient's diabetes is, in fact, "statin-induced."

Q. Well, what is statin induced diabetes and how does it – how does it present?
A. Well, statin induced diabetes would present as regular diabetes, but from a drug, specifically a statin drug.
* * *
Q. So there's nothing, no unique symptom that a person who has what you call statin induced diabetes has than a person who has non-statin induced diabetes wouldn't have?
A. No.
* * *
Q. Is there any single clinical feature that is different in what you call statin induced diabetes than what you find in patients who have non-statin induced diabetes?
A. No.
* * *
Q. Is there any validated test or procedure that you could perform that would distinguish what you call statin induced diabetes from non-statin induced diabetes?
A. No.

Id. at 160:4-162:22. In a room filled with diabetics, Dr. Handshoe cannot distinguish between patients with "statin-induced" and non-"statin-induced" diabetes.

Q. Could you walk into a room of 100 patients with diabetes and pick out the ones who have what you call statin induced diabetes versus the non-statin induced diabetics?
A. No.
Q. Could you even do that if there were ten people in the room?
A. No.
Q. Could you do it between two people?
A. No.

Id. at 162:8-17. In sum, Dr. Handshoe applies a litigation-driven standard in this courtroom that he has never applied in his professional practice. "[O]ne of the abuses, at which *Daubert* and its sequelae are aimed … is the hiring of [experts] to testify for a fee to propositions that they have not arrived at through the methods that they use when they are doing their regular professional work rather than being paid to give an opinion helpful to one side in a lawsuit." *Braun v. Lorillard Inc.*, 84 F.3d 230, 235 (7th Cir. 1996); *see also Allen v. Pa. Eng'g Corp.*, 102 F.3d 194, 198 (5th Cir. 1999); *Watkins v. Telsmith, Inc.*, 121 F.3d 984, 992 (5th Cir. 1997). The Supreme Court has emphasized that "the importance of *Daubert*'s gatekeeping requirement … is to make certain that an expert … employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999). Dr. Handshoe's testimony thus cannot pass the *Daubert* test for reliability.

A. Dr. Handshoe Improperly Bases His Opinion on Temporal Proximity

In addition to the many infirmities in Dr. Handshoe's methodology that are discussed below, Dr. Handshoe's specific causation opinions are unreliable because they are based on little more than the temporal relationship between Plaintiffs' ingestion of Lipitor and their subsequent diabetes diagnoses. Regardless of what other risk factors a Plaintiff may have, "the most important variable" for Dr. Handshoe is the temporal proximity between use of the statin and the diagnosis of diabetes. Handshoe *Daniels* Tr. (Ex. 6) at 180:5-16; 192:9-24. According to Dr. Handshoe, if a Plaintiff with multiple diabetes risk factors starts taking Lipitor and is later diagnosed with diabetes, the leap from temporal proximity to causation is a simple one.

Q. So that's my question, how do you tell who did get what you call statin induced diabetes versus those who took a statin, but got diabetes for some other reason. Can you tell those people apart?

> A. If you're a woman and you have premorbid conditions ***and you're prescribed this drug*** and then you pop up with diabetes, ***one plus one equals two***.

Handshoe *Daniels* Tr. (Ex. 6) at 160:9-16; *see also id.* at 164:11-19. He unequivocally admits that there is no other critical part of his methodology beyond the temporal relationship.

> Q. So regardless of what her risk factors are, how many there are or how strong they are, am I correct that ***what you're really focusing on is the temporal relationship between statin use and diagnosis of diabetes?***
> A. ***That's correct.***
> Q. So here's Ms. Daniels, she has a number of independent powerful risk factors for diabetes, but essentially, ***your logic is she*** didn't – she had those, but ***didn't have diabetes until after she began taking the statin?***
> A. ***That's correct.***
> Q. Therefore, under your method, it is statin induced diabetes?
> A. Correct.
> Q. ***Am I missing any other critical fact or critical logical step in your methodology?***
> A. ***No.***

Id. at 199:19-200:11.

Dr. Handshoe's exclusive focus on temporal proximity pervades every aspect of his opinion. For example, when asked how his differential diagnosis accounted for Plaintiffs' pre-existing independent risk factors, Dr. Handshoe could only cite temporal proximity.

> Q. How does your methodology account for the presence of risk factors other than statins in an individual case like Ms. Daniels?
> A. ***She*** has multiple risk factors for diabetes, ***did not have diabetes prior to ingestion of the drug and subsequently developed diabetes***.

Handshoe *Daniels* Tr. (Ex. 6) at 174:14-20. He cited temporal proximity when purporting to account for Ms. Daniels's obesity, explaining: "She did not have diabetes until she took the drug for a year. So the way I look at this and put it together, again, she had statin induced diabetes." Handshoe *Daniels* Tr. (Ex. 6) at 199:10-18. He cited temporal proximity when attempting to account for Ms. Hempstead's age as a risk factor, stating that "[o]nce she started taking Lipitor over time is when she developed her glucose intolerance/prediabetes and development of diabetes." Handshoe *Hempstead* Tr. (Ex. 41) at 144:9-23. He relied on temporality again when he claimed he accounted for both women's family history, saying: "due to the temporal

relationship of her high-dose Lipitor ingestion, I believe that her pre-diabetes was caused by her Lipitor ingestion and not her family history." Handshoe *Daniels* Rpt. (Ex. 7) at 11; *see also* Handshoe *Hempstead* Tr. (Ex. 41) at 84:15-85:3. And he purported to account for all of Ms. Hempstead's other risk factors and conclude that Lipitor was "the major driver, if not the only driver of her diabetes" because after taking Lipitor, she was diagnosed with diabetes. Handshoe *Hempstead* Tr. (Ex. 41) at 236:15-237:9, 238:7-17, 238:23-239.

When asked how he could diagnose a case of "statin-induced" diabetes, which presents exactly the same as non-"statin-induced" diabetes, Dr. Handshoe could only rest on temporality.

> Q. So is there any sign, feature, test result, symptom, anything at all that distinguishes statin induced diabetes, as you call it, from diabetes that's not statin induced?
> A. ***She would*** have to have the right clinical risk factors, the right gender, ***be prescribed the drug, then develop diabetes or prediabetes***.

Handshoe *Daniels* Tr. (Ex. 6) at 160:9-16.

When asked why he did not compare the relative risk of statins to the much higher relative risks of Plaintiffs' other, pre-existing diabetes risk factors, Dr. Handshoe claimed that the temporal relationship between Plaintiffs' ingestion of Lipitor and subsequent diabetes diagnoses renders such analyses unnecessary.

> Q. My question is, is there some element of your methodology that weighs or compares the risk that's been reported for statin use to the other risk factors that are present in a patient like Mrs. Daniels?
> A. There's – again, I'm not sure what you're – my methodology – in other words, she had multiple risk factors for diabetes as we discussed. ***She was exposed to the statin drug. She subsequently developed diabetes***.

Handshoe *Daniels* Tr. (Ex. 6) at 175:11-20; *see also id.* at 133:12-134:13.

In contrast to Dr. Handshoe, Plaintiffs' other experts, Drs. Singh and Quon, admit that just because a patient takes Lipitor and is then diagnosed with diabetes does not mean that Lipitor caused her diabetes. Singh Tr. (Ex. 3) at 356:6-14; Quon Tr. (Ex. 2) at 75:6-12; 85:22-86:5. Courts consistently have held that the mere temporal relationship between exposure to a substance and the development of a medical condition is insufficient – and, indeed, fallacious – scientific proof of causation. For example, the Eleventh Circuit held that "proving a ***temporal***

relationship between taking [a drug] and the onset of symptoms does not establish a ***causal*** relationship. In other words, simply because a person takes drugs and then suffers an injury does not show causation. Drawing such a conclusion from temporal relationships leads to the blunder of the *post hoc ergo propter hoc* fallacy" – after this, therefore because of this. *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1243 (11th Cir. 2005); *accord Kilpatrick*, 613 F.3d at 1343. Likewise, the Fifth Circuit has held that "the temporal connection between exposure to chemicals and an onset of symptoms, standing alone, is entitled to little weight in determining causation." *Moore v. Ashland Chem. Inc.*, 151 F.3d 269, 278 (5th Cir. 1998). Inferring causation from temporality "is not an exercise in scientific logic but in the fallacy of *post-hoc propter-hoc* reasoning, which is as unacceptable in science as in law." *Black v. Food Lion, Inc.,* 171 F.3d 308, 313 (5th Cir. 1999).

Courts in this Circuit have also held that a purported differential diagnosis that is premised on temporal proximity is inadmissible. *Roche v. Lincoln Prop. Co.*, 278 F. Supp. 2d 744, 750 (E.D. Va. 2003). As the Fourth Circuit explained in *Westberry*, "the mere fact that two events correspond in time does not mean that the two necessarily are related in any causative fashion." 178 F.3d at 265. In *Westberry*, the court held that temporality was sufficient due to "compelling" circumstances not present here, namely the plaintiff's treating physician testified that the plaintiff's sinus disease began shortly after occupational exposure to an alleged toxin, improved when the physician experimented with keeping him from work, and worsened when the plaintiff returned to work. *Id.* But the Eleventh Circuit cogently explained that *Westberry*'s narrow holding cannot be extended to diabetes cases like this one. *See Guinn*, 602 F.3d at 1254.

Two cases involving a diagnosis of diabetes and use of the drug Seroquel are very much on point. In *Guinn*, the Eleventh Circuit held that the plaintiff's specific causation expert "did not adequately consider possible alternative causes simply by noting the temporal proximity between [plaintiff's] ingestion of [the drug] and subsequent development of diabetes." *Id.* at 1255. The court explained that "several factors" in that case "make [temporal proximity] especially unreliable" as grounds for a specific causation opinion. *Id.* at 1254. The *Guinn* court

emphasized the fact that "the development of diabetes occurs gradually over many years" and that "numerous other risk factors for diabetes make it hard to draw any inferences from the temporal proximity" alone. *Id.* "Because Guinn was diagnosed with diabetes only four years after beginning to take [the drug], the temporal relationship in this case does not provide strong evidence of causation; in fact, it appears to equally indicate that Guinn may have already developed diabetes before ever taking [the drug]." *Id.*

Likewise, in *Haller* – another Seroquel diabetes case – the district court rejected an expert's purported "differential diagnosis" that was based on little more than temporality. Like Dr. Handshoe, the specific causation expert in *Haller* conceded that the plaintiff had multiple risk factors that could have caused his diabetes even if he had never taken the defendant's drug. *See Haller*, 598 F. Supp. 2d at 1302. "Despite these admissions, [the expert] was curiously confident in his opinion that [the drug] was a 'substantial contributing cause' of [the plaintiff's] diabetes." *Id.* at 1303. During his deposition, the expert explained "that other risk factors had not yet caused diabetes until [the drug] was added to the mix." *Id.* The *Haller* court rejected this methodology as "temporal proximity in disguise" and held that the expert "has not met the standard of reliability required under *Daubert*." *Id.*

So, too, here. Ms. Hempstead and Ms. Daniels were both diagnosed with diabetes within approximately five years after taking Lipitor. Handshoe *Hempstead* Rpt. (Ex. 39) at 9; Handshoe *Daniels* Rpt. (Ex. 7) at 9. But as Dr. Gale admits, the progression from disease initiation until diagnosis is "a long, slow process" that takes "***at least a decade*** or so." Gale Tr. (Ex. 1) at 174:5-175:18; 183:6-12. A diagnosis of diabetes is "not a new injury" but rather a "milestone" in a progressive disease process. *Id.* at 184:1-8.

"Without exposure before the disease, causation cannot exist." *Reference Manual on Scientific Evidence* (3d ed. 2011) ("*RM* (3d)") at 601. "[T]he exposure … must not just precede the outcome, but must do so by a period of time that is consistent with biologic mechanisms," for "[a] disease process that precedes the exposure cannot be caused by that exposure." Hennekens Rpt. (Ex. 16) at 31. As the Eleventh Circuit explained in *Guinn*, "[t]emporal proximity is

generally not a reliable indicator of a causal relationship," particularly where, as here, "the development of diabetes occurs gradually over many years," but is diagnosed just a handful of years after taking the drug. 602 F.3d at 1254. Just as the court there properly struck the plaintiff's expert causation testimony, this Court should strike Dr. Handshoe's testimony here.

B. Dr. Handshoe Did Not Conduct a True Differential Diagnosis

In terms of assessing causation, what some might call a "differential diagnosis" is more accurately termed a "differential etiology." *RM* (3d) at 617 n.211; *Tamraz*, 620 F.3d at 674; *Westberry*, 178 F.3d at 262. Whichever label is applied, "[t]his method involves a process of compiling, or ruling in, a comprehensive list of possible causes that are generally capable of causing the illness or disease at issue, and then systematically and scientifically ruling out specific causes until a final, suspected cause remains." *Kilpatrick*, 613 F.3d at 1342; *see also Cooper*, 259 F.3d at 200 (quoting *Westberry*, 178 F.3d at 261). "In order to correctly apply this methodology, [the expert] must have compiled a comprehensive list of potential causes of [the plaintiff's] injury and must have explained why potential alternative causes were ruled out." *Kilpatrick*, 613 F.3d at 1342-43. Here, Dr. Handshoe fails to do so.

While a "properly conducted" differential diagnosis can pass *Daubert* muster, "'an expert does not establish the reliability of his techniques or the validity of his conclusions simply by claiming that he performed a differential diagnosis on a patient.'" *Guinn*, 602 F.3d at 1253 (citation omitted). The law instructs that "'simply claiming that an expert used the "differential diagnosis" method is not some incantation that opens the *Daubert* gate.' Calling something a 'differential diagnosis' or 'differential etiology' does not by itself answer the reliability question but prompts three more: (1) Did the expert make an accurate diagnosis of the nature of the disease? (2) Did the expert reliably rule in the possible causes of it? (3) Did the expert reliably rule out the rejected causes? If the court answers 'no' to any of these questions, the court must exclude the ultimate conclusion reached." *Tamraz*, 620 F.3d at 674 (citations omitted). Here, Dr. Handshoe failed to properly rule in and rule out the risk factors for diabetes in both Plaintiffs.

The broad scope of Dr. Handshoe's disregard of many well-recognized risk factors for diabetes shows that he did not follow any generally accepted process for ruling in or ruling out other risk factors for diabetes, but instead simply reached a pre-ordained litigation opinion without reference to any objective scientific or medical methodology. In *Haller*, the MDL court considered and excluded similar specific causation opinions regarding diabetes. There, the court observed that the plaintiff "had many pre-existing and concurrent factors that could have caused his diabetes" and that "simple logic and common sense dictated that [the expert] conduct some inquiry concerning whether Haller was continuing these habits and, if so, what potential role they played in Haller becoming diabetic." 598 F. Supp. 2d at 1295. The expert's failure to do so was fatal to the admissibility of his opinion. *Id.* It is equally fatal to Dr. Handshoe's opinion here.

C. Dr. Handshoe Fails to Rule In Plaintiffs' Well-Recognized Risk Factors

The "ruling in" stage of Dr. Handshoe's methodology is fatally flawed. If a specific causation expert does not "reliably rule in the possible causes" of the Plaintiffs' illness, then "the court must exclude the ultimate conclusion reached." *Tamraz*, 620 F.3d at 674 (citations omitted). The Fourth Circuit has held that a "differential diagnosis that fails to take serious account of other potential causes may be so lacking that it cannot provide a reliable basis for an opinion on causation." *Cooper*, 259 F.3d at 202 (quotations omitted). Here, Dr. Handshoe fails to properly consider many of the most obvious of the well-recognized risk factors for Plaintiffs' diabetes. Having failed to rule these in as alternative risk factors, he could not rule them out as independent causes of Plaintiffs' diabetes. His failure to do so renders his opinion inadmissible.

***Weight Gain*:** While Dr. Handshoe recognizes obesity as a risk factor for diabetes, his failure to rule in Plaintiffs' adult weight gain as an alternative risk factor for diabetes is a glaring error in his methodology. He admits that both Plaintiffs had significant adult weight gain. Handshoe *Daniels* Tr. (Ex. 6) at 196:4-8, 135:17-23; Handshoe *Hempstead* Tr. (Ex. 41) at 107:11-14. Adult weight gain is a well-recognized risk factor for diabetes, and a person need

not be obese to be at increased risk for diabetes.[24] Yet he did not know whether adult weight gain was a risk factor distinct from obesity, and purported to "reserve comment" on the matter. Handshoe *Hempstead* Tr. (Ex. 41) at 108:2-7. He further claimed that it would not be a risk factor if the weight gain was slow, but he could not cite any support in the medical literature for this assertion. *Id.* at 115:12-17. Instead, he rested that opinion on his "clinical judgment," *see id.*, which is nothing more than a euphemism for his own say so. *See Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997); *Alevromagiros v. Hechinger Co.*, 993 F.2d 417, 421 (4th Cir. 1993); *Viterbo*, 826 F.2d at 424. "A witness who invokes 'my expertise' rather than analytic strategies widely used by specialists is not an expert as Rule 702 defines that term." *Zenith Elecs. Corp. v. WH-TV Broad. Corp.*, 395 F.3d 416, 419 (7th Cir. 2005); *see also Tamraz*, 620 F.3d at 670; *Rutigliano v. Valley Bus. Forms*, 929 F. Supp. 779, 786 (D.N.J. 1996). Here, Dr. Handshoe relies on personal anecdote and personal opinion, not scientific knowledge.

Yet Dr. Handshoe did not dispute that adult weight gain is a risk factor for diabetes when he was presented with the landmark Nurses Health Study,[25] with which he admitted he was not familiar but had no reason to question. Handshoe *Daniels* Tr. (Ex. 6) at 204:11-18, 208:11-21. Based on the data in that study, he agreed that Ms. Daniels's age-adjusted BMI gave her a relative risk of being diagnosed with diabetes that was a 4000%, or ***40.3***-fold, increase compared to women who did not have that weight gain. Handshoe *Daniels* Tr. (Ex. 6) at 207:12-20.

In evaluating the risk attributable to Lipitor, Dr. Handshoe relied on the 1.37 relative risk reported in the Waters study,[26] even though that study only involved an 80 mg dose of Lipitor that neither Ms. Daniels nor Ms. Hempstead took. Initially, Dr. Handshoe's attempt to show causation based on a study involving a higher dose than either Plaintiff ever took is unreliable,

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[24] Colditz et al., *Weight Gain as a Risk Factor for Clinical Diabetes Mellitus in Women*, 122 Annals of Internal Med. 484, 484-85 (1995) (Ex. 46).

[25] *See id.*

[26] Waters et al., *Predictors of new-onset diabetes in patients treated with atorvastatin: results from 3 large randomized clinical trials*, 57 J. Am. Coll. Cardiol. 1535, 1535 (2011) (Ex. 14).

since "[t]o establish specific causation," an expert must show that the individual's dose "was of sufficient magnitude and duration to be capable of producing the alleged effect." *Downs v. Perstorp Components, Inc.*, 126 F. Supp. 2d 1090, 1095 (E.D. Tenn. 1999). When asked to compare that risk to the 40.3 relative risk attributable to weight gain, he said "[t]hey're pretty equivalent, 37, 40." Handshoe *Daniels* Tr. (Ex. 6) at 215:24-216:8. Focusing on the wrong side of the decimal point, his math is wrong by a huge margin of error: the 40.3 (4030%) relative risk for Ms. Daniels's weight gain is 108 times the size of Waters' reported 1.37 (37%) relative risk for patients who took the high 80 mg dose of Lipitor, which neither Plaintiff did. That Dr. Handshoe disregards a risk factor that vastly eclipses the relative risk allegedly attributable to Lipitor is fatal to his methodology.

***Hypertension*:** Dr. Handshoe admits that hypertension is a well-recognized risk factor for diabetes. Handshoe *Daniels* Tr. (Ex. 6) at 129:21-130:5. He was aware of Ms. Daniels's preexisting hypertension, *see id.* at 135:24-25, and of Ms. Hempstead's long-term treatment for hypertension. Handshoe *Hempstead* Tr. (Ex. 41) at 159:6-8. Yet in neither case does his expert report consider hypertension as an alternative risk factor for diabetes. Handshoe *Hempstead* Tr. (Ex. 41) at 180:17-24. At his deposition, he could not even address the comparative risk that hypertension poses for diabetes, as compared to statins. Handshoe *Daniels* Tr. (Ex. 6) at 132:12-17. His failure to consider hypertension renders his opinion methodologically unreliable.

***Metabolic Syndrome*:** Dr. Handshoe admits that metabolic syndrome is a well-recognized, powerful risk factor for diabetes. Handshoe *Daniels* Tr. (Ex. 6) at 116:24-117:19; 236:3-7; Handshoe *Hempstead* Tr. (Ex. 41) 176:21-24. He admits that Ms. Daniels and Ms. Hempstead met the criteria for metabolic syndrome before taking Lipitor. Handshoe *Hempstead* Tr. (Ex. 41) at 177:8-11; Handshoe *Daniels* Tr. (Ex. 6) at 233:21-235:4. He even admits that the cluster of risks in metabolic syndrome increases the risk of diabetes more than each single risk by itself. Handshoe *Hempstead* Tr. (Ex. 40) at 176:6-15. Yet Dr. Handshoe ignores this alternative risk factor in reaching his specific causation opinion as to both Ms. Daniels and Ms.

Hempstead. *See* Handshoe *Daniels* Tr. (Ex. 6) at 235:5-7; Handshoe *Hempstead* Tr. (Ex. 41) at 176:16-20. He provided no reason for doing so.

***Ethnicity*:** Although Dr. Handshoe acknowledged the increased risk of diabetes associated with Ms. Hempstead's partial African-American ethnicity, he tried to downplay it by noting that her Choctaw Indian ethnicity "in [his] experience is not associated with increased diabetes risk," "[p]lus she had Caucasian blood from a French ancestry." Handshoe *Hempstead* Tr. (Ex. 41) at 140:20-141:6. Yet Dr. Handshoe did not investigate the incidence of diabetes in Choctaw Indians. Instead, he based his opinion on his "clinical experience of working in rural Mississippi where the Choctaw Nation is from," where he "did not see an increase incidence of diabetes in Choctaw Indians." *Id.* at 139:15-23. Because he "did not specifically do a literature search on Choctaw Indian and diabetes," *id.* at 141:21-25, he did not identify a 1993 study in Diabetes Care[27] reporting a 6.5-fold increase in diabetes in Choctaw Indians. *Id.* at 204:16-205:13. He tried to distinguish this study by noting that Ms. Hempstead was multi-ethnic rather than pure Choctaw and older than the average in the study population. *Id.* at 206:12-207:3. Yet both of these distinctions cut against him. Since Ms. Hempstead's African American ethnicity is also a risk factor for diabetes and since she was older than the study population, that increases, rather than decreases, her comparative risk. Dr. Handshoe's *ipse dixit* "clinical judgment" and ignorance of medical literature cannot justify his failure to properly consider this risk factor.

***Smoking History*:** Dr. Handshoe admits that both Plaintiffs have a history of smoking, Handshoe *Daniels* Tr. (Ex. 6) at 227:6-19; Handshoe *Hempstead* Tr. (Ex. 41) at 146:14-147:4, which was up to a pack a day for Ms. Daniels over 30 years. Plaintiffs' other experts agree that smoking is a risk factor for diabetes,[28] but Dr. Handshoe did not consider either Plaintiff's smoking history. Dr. Handshoe initially testified that he disagreed with the Surgeon General's statement that smoking causes diabetes, *see* Handshoe *Daniels* Tr. (Ex. 6) at 227:6-19, 228:14-229:3, though he had not examined the Surgeon General's evidence. *Id.* at 229:17-23; 230:14-

[27] Johnson & Strauss (1993) (Ex. 42).
[28] Gale Tr. (Ex. 1) at 76:10-77:9; Murphy Tr. (Ex. 18) at 50:22-52:5.

21. On the evening between his two depositions, Dr. Handshoe looked into the issue. Handshoe *Hempstead* Tr. (Ex. 41) at 146:14-147:4. On day two, he opined that "[t]here is some studies that suggest that [smoking] does" increase the risk of diabetes, and "some studies that suggest it doesn't," and because the risk in women is "much smaller than men" it was "completely insignificant" for Ms. Hempstead's smoking history. *Id.* He admitted, however, that he did not cite any of this unnamed medical literature in his report or rely on it when reaching his opinion. *Id.* at 147:5-9. This "moving target" opinion is not science, but advocacy. *Haller*, 598 F. Supp. 2d at 1296-97. The Fourth Circuit has affirmed the exclusion of specific causation testimony where an expert refused to rule in the plaintiff's smoking as a well-recognized alternative cause of the plaintiff's injury. *See Cooper*, 259 F.3d at 202. This Court should do so as well here.

D. Dr. Handshoe Fails to Rule Out Plaintiffs' Well-Recognized Risk Factors

While Dr. Handshoe pays lip service to the concept of "differential diagnosis," his testimony reveals he did not actually perform one. In his expert reports, Dr. Handshoe claimed to have ruled out other pre-existing risk factors as independent causes of Plaintiffs' diabetes. *See* Handshoe *Daniels* Rpt. (Ex. 7) at 7-11; Handshoe *Hempstead* Rpt. (Ex. 39) at 7-11. But at his deposition, Dr. Handshoe freely admitted that he did not actually rule out ***any*** risk factors.

Q. And ultimately at the end of the day ***you don't actually rule out those other risk factors, do you***?
A. ***No***. The risk factors are vitally important because the science says most of the people that develop statin induced diabetes have all of these risk factors.
Q. Is there any ruling out of risk factors at all?
A. The more risk factors you have the higher likelihood that you're going to develop statin induced diabetes.
Q. Right. But as far as your methodology goes, there's not really any ruling out of risk factors, is there?
A. The more risk factors you have the higher the risk of a drug induced or statin induced diabetes.
Q. I understand. But to get it down to the point where you can say, ah-ha, this is a case of statin induced diabetes, ***you don't actually rule out any of the other risk factors***, do you?
A. ***No***.
Q. They all roll in together?
A. That's correct.

Handshoe *Daniels* Tr. (Ex. 6) at 177:16-178:16; *see also id.* at 198:9-17.

Instead of scientifically ruling out alternative causes, Dr. Handshoe opined that the "totality" of Plaintiffs' risk factors had an "additive" effect that collectively caused their diabetes. *Id.* at 133:12-20, 219:11-220:4, 224:2-11. Due to its inherent unreliability, the Eleventh Circuit rejected an identical methodology used by an expert in *Guinn*, where the plaintiff's specific causation expert "testifi[ed] that '[a]ll the [risk] factors [for diabetes] work together.'" 602 F.3d at 1225. The Eleventh Circuit recognized this for the evasion that it is:

> Dr. Marks ... testif[ied] that "[a]ll the [risk] factors [for diabetes] work together." Here Dr. Marks appears to be contending that since diabetes can have multiple concurrent causes, she need not analyze the role played by each cause.
>
> An expert, however, cannot merely conclude that all risk factors for a disease are substantial contributing factors in its development. "The fact that exposure to [a substance] may be a risk factor for [a disease] does not make it an actual cause simply because [the disease] developed."

Id. (citation omitted). "[T]he presence of a known risk factor," let alone a contested risk factor like Lipitor, "is not a sufficient basis for ruling out" alternative causes, including idiopathic causes, of a disease. *Perry v. Novartis Pharm. Corp.*, 564 F. Supp. 2d 452, 470 (E.D. Pa. 2008); *accord Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1162 (E.D. Wash. 2009).

The law instructs that where, as here, an expert "has admitted that [plaintiff's] symptoms could have numerous causes," he cannot "simply pick[] the cause that is most advantageous to [plaintiff's] claim." *Viterbo*, 826 F.2d at 424. The Fourth Circuit does not accept opinions from experts simply because the "expert says it is so." *Alevromagiros*, 993 F.2d at 421 (quoting *Viterbo*). Nor does the Supreme Court: "*ipse dixit*" does not suffice. *Joiner*, 522 U.S. at 146.

E. Dr. Handshoe's Methodology Fails *Daubert*'s Reliability Factors

Daubert sets forth four non-exclusive factors to consider when assessing the reliability of an expert's methodology: testing, peer review or publication, known or potential rate of error, and general acceptance in the scientific community. *Daubert v. Merrell Dow Pharms., Inc.,* 509 U.S. 579, 593-94 (1993). Dr. Handshoe's methodology fails to satisfy any of these factors. He

admits there are no published or generally accepted criteria for using differential diagnosis to determine the cause of a patient's diabetes.

> Q. Now, has this methodology of using differential diagnosis to identify patients with statin induced diabetes been written down in any peer reviewed scientific article or textbook or journal?
> A. Not that I've encountered.
> Q. Are you aware of any place where the steps of your differential diagnosis methodology to identify statin induced diabetes has been written down other than in your report?
> A. No.
> Q. Has this differential diagnosis methodology been validated to identify statin induced diabetes?
> A. Not as far as I'm aware.

Handshoe *Daniels* Tr. (Ex. 6) at 171:22-172:18. Dr. Handshoe further admits that his methodology has never been tested and has no known rate of error.

> Q. So would you agree that a scientifically validated methodology is one that when it's employed by different people to the same set of facts or evidence, it should produce the same results?
> A. Usually, yes.
> Q. And if two or more people apply the same methodology to the same set of fact and evidence, but reach different results, then it raises some questions about the validity of the methodology, right?
> A. Correct.
> Q. Would you agree that the methodology is not scientifically valid if it always reaches the same result time and time again when applied to different sets of facts?
> A. Correct.
> Q. Dr. Handshoe, what's the rate of error for your differential diagnosis methodology of identifying statin induced diabetes?
> A. This is a sample of one for this particular case, so that has not been calculated.
> Q. So it's impossible to say what the rate or potential rate of error is for your methodology?
> A. Correct.

Id. at 172:19-173:19. Among other things, when one cannot "determine [a methodology's] known or potential rate of error," it "can hardly ... meet[] the *Daubert* requirement of evidentiary reliability." *In re TMI Litig.*, 193 F.3d 613, 669 (3d Cir. 1999), *amended*, 199 F.3d 158 (3d Cir. 2000). Dr. Handshoe's "analysis by assumption could lead to an unacceptable potential for error" and is inadmissible. *Marsh v. W.R. Grace & Co.*, 80 F. App'x 883, 887 (4th Cir. 2003).

In addressing the basis of his opinions, Dr. Handshoe repeatedly invokes his so-called "clinical judgment," which does nothing more than obscure his analysis. Dr. Handshoe admits that patients who supposedly have "statin-induced" diabetes present just like patients with non-"statin-induced" diabetes. Thus, he falls back on his so-called "clinical judgment" in claiming that Plaintiffs have "statin-induced" diabetes, Handshoe *Daniels* Tr. (Ex. 6) at 263:15-19; *see also id.* at 274:11-24 – *i.e.*, that Lipitor was the "major driver" of their diabetes.

> Q. ... Are you relying on anything in the medical or scientific literature to support your opinion that – where you ruled out her heritage as increasing her risk of diabetes?
> A. It is based on ***my clinical judgment*** and review of the medical literature, correct.
> Q. But is there anything in the medical literature that you're relying on?
> A. No. No.
> * * *
> Q. But you don't actually believe that any of those risk factors contributed to her increased blood sugar in any way; is that correct?
> A. As I've said several and multiple times earlier today, I assessed all her risk factors, I felt that they were not significant to ***my clinical judgment***. I thought the ingestion of her drug was the major driver, if not the only driver of her diabetes. She had normal blood sugars, took this drug for three to four years and developed Type 2 Diabetes.

Handshoe *Hempstead* Tr. (Ex. 41) at 141:7-20, 236:15-237:1; *see also id.* at 112:21-113:15, 115:12-17, 139:15-23, 143:12-16.

Dr. Handshoe's reliance on his so-called "clinical judgment" has no fit with his causation opinion. "[T]here is a fundamental distinction between [a physician's] ability to render a medical diagnosis based on clinical experience and her ability to render an opinion on causation of [a plaintiff's] injuries." *Wynacht v. Beckman Instruments, Inc.*, 113 F. Supp. 2d 1205, 1209 (E.D. Tenn. 2000). "The ability to diagnose medical conditions is not remotely the same ... as the ability to deduce, delineate, and describe, in a scientifically reliable manner, the causes of those medical conditions." *Id.*; *see also Sutera v. Perrier Grp. of Am., Inc.*, 986 F. Supp. 655, 667 (D. Mass. 1997). By invoking his "clinical judgment," Dr. Handshoe demonstrates that his reasoning is subjective and that it cannot be described in a scientifically reliable manner. His reliance on it is simply a euphemism for his say so – *i.e.*, his inadmissible "*ipse dixit*." *Joiner*,

522 U.S. at 146. This is especially true here where these issues are not part of Dr. Handshoe's clinical practice. An expert's "clinical judgment does not provide an adequate basis for an opinion on an issue foreign to [the expert's] clinical practice. This is the type of subjective belief and unsupported speculation that *Daubert* guards against." *Nelson v. Matrixx Initiatives*, 2012 WL 3627399, at *12 (N.D. Cal. Aug. 21, 2012), *aff'd*, 592 F. App'x 591 (9th Cir. 2015).

Dr. Handshoe never diagnosed one of his own patients with "statin-induced" diabetes. Handshoe *Daniels* Tr. (Ex. 6) at 165:8-10, 165:15-17. He has never determined that any of his patients would not have developed diabetes if that patient had not taken a statin. *Id.* at 88:25-89:12; 165:18-22. He never told a patient he believed statins caused or worsened their diabetes. *Id.* at 89:13-20; 165:11-14. He never saw a patient with "statin-induced" diabetes with his own eyes. *Id.* at 166:9-11. The only time that he has used a so-called "differential diagnosis" to identify what he calls "statin-induced" diabetes is in this litigation. *Id.* at 184:7-11.

Dr. Handshoe's "clinical judgment" as support for his litigation-driven opinion of "statin-induced" diabetes does not employ the "intellectual rigor that characterizes the practice of the expert in the relevant field." *Kumho*, 526 U.S. at 152. He proffers an untested methodology that he created for this litigation – a "significant fact weighing against admitting the testimony." *Wehling v. Sandoz Pharms. Corp.*, 162 F.3d 1158, 1998 WL 546097, at *3 (4th Cir. 1998).

III. DR. HANDSHOE'S OPINIONS DO NOT SUBSTANTIVELY ADDRESS SPECIFIC CAUSATION

A. Dr. Handshoe Admits that He Cannot Show But-For Causation

Dr. Handshoe's opinion is inadmissible because he admits that he cannot satisfy an essential element of proof of specific causation – whether, but for Lipitor, Plaintiffs would have developed diabetes.

> Q. Can you answer my question. You cannot say that but for taking Lipitor, she wouldn't have been diagnosed with diabetes at some point?
> A. ***Nobody can say that.***

Handshoe *Daniels* Tr. (Ex. 6) at 276:12-16. Yet "but-for" causation is essential to Plaintiffs' claims: they must show that they would have not developed diabetes had they not taken Lipitor.

For Ms. Daniels, Colorado law requires proof that the conduct at issue in a "natural and continued sequence, unbroken by any efficient, intervening cause, produce[s] the result complained of, ***and without which the result would not have occurred***." *N. Colo. Med. Ctr. v. Comm. on Anticompetitive Conduct*, 914 P.2d 902, 908 (Colo. 1996) (emphasis added); *Reigel v. SavaSeniorCare L.L.C.*, 292 P.3d 977, 987 (Colo. Ct. App. 2011); *June v. Union Carbide Corp.* 577 F.3d 1234, 1244-45 (10th Cir. 2009). Likewise, for Ms. Hempstead, Missouri law holds that "satisfaction of the 'but for' test is an ***absolute minimum*** for causation." *Vaughn v. N. Am. Sys., Inc.*, 869 S.W.2d 757, 759 (Mo. 1994) (emphasis added, citation omitted); *see also City of St. Louis v. Benjamin Moore & Co.*, 226 S.W.3d 110, 114 (Mo. 2007).

Dr. Handshoe's opinions do not address but-for causation except through conclusory assertions that are belied by his deposition testimony. He opines that Lipitor was a "substantial contributing factor," "but for" which Ms. Daniels and Ms. Hempstead would not have developed diabetes. Handshoe *Daniels* Rpt. (Ex. 7) at 3, 4, 11, 14; Handshoe *Hempstead* Rpt. (Ex. 39) at 3, 4, 7, 11, 14. But he admits that he does not understand what the term "but for" means.

> Q. Were you able to determine in those cases, take family history for instance, that but for the patient's family history, that patient would not have developed Type 2 diabetes?
> A. It's the "but for" question, that's the – again, re-explain it.
> Q. Sure. And I'm just kind of reading from your report.
> A. Right.

Handshoe *Daniels* Tr. (Ex. 6) at 189:4-12; *see also id.* at 276:7-11. To be sure, Dr. Handshoe testified that Lipitor "caused" both Plaintiffs' diabetes. *Id.* at 135:6-16; Handshoe *Hempstead* Tr. (Ex. 41) at 116:16-21. Conclusory assertions aside, on the fundamental question of specific causation, Dr. Handshoe states that "[n]obody can say" whether Plaintiffs would have been diagnosed with diabetes but for taking Lipitor. Handshoe *Daniels* Tr. at 276:12-16.

Dr. Handshoe admits that Ms. Daniels and Ms. Hempstead had major pre-existing diabetes risk factors. *Id.* at 135:17-136:3, 240:9-15; Handshoe *Hempstead* Tr. (Ex. 41) at 39:25-40:10. He further admits that such high-risk patients "are among the most likely to go on to develop diabetes ... regardless of whether they use statins or not." Handshoe *Daniels* Tr. (Ex. 6)

at 114:17-115:8. He admits that "[m]any patients with risk factors like Ms. Daniels who have never in their lives taken a statin are diagnosed with Type 2 diabetes every day." *Id.* at 137:11-15; *see* Handshoe *Hempstead* Tr. (Ex. 41) at 238:18-22. It would not surprise Dr. Handshoe if a patient exactly like Ms. Daniels, but who had never taken a statin, were diagnosed with diabetes. Handshoe *Daniels* Tr. (Ex. 6) at 226:2-23.

Dr. Handshoe opines that because Ms. Daniels and Ms. Hempstead were high-risk patients who also took statins, they are the type of "folks that develop statin induced diabetes based on science." Handshoe *Daniels* Tr. (Ex. 6) at 175:21-176:2. But Dr. Handshoe's testimony reveals the wide, unbridged gap between his opinion that Lipitor may have caused Plaintiffs' diabetes and his conclusory assertions that Lipitor in fact did so in these two Plaintiffs.

Presented with the hypothetical of 20 patients with identical risk factors, medical history, and statin use, all of whom went on to develop diabetes, Dr. Handshoe admitted that he could not tell which of those women would have developed diabetes even if they had never taken statins.

> Q. All right. Let's take my twenty women again. Twenty identical women all of who begin Lipitor at exactly the same dose, taken at exactly the same length of time and are diagnosed on exactly the same day, they you all have exactly the same risk factors independent of statin use. Given that temporal relationship that they begin taking Lipitor and are subsequently diagnosed with diabetes, would you say that all of those women developed statin induced diabetes?
> A. No.
> Q. And again, is there any way you can tell the difference?
> A. No.

Handshoe *Daniels* Tr. (Ex. 6) at 202:12-203:1; *see also id.* at 181:13-23. The impossibility of identifying cases of "statin-induced" diabetes in such a set of women is plain from Dr. Handshoe's admission that "statin-induced" diabetes has no unique "clinical symptoms," no "single clinical feature," no recognized "diagnostic standards," and "would present as regular diabetes." *Id.* at 159:6-9, 159:25-160:8, 161:1-11, 162:3-22. Thus, Dr. Handshoe cannot answer the fundamental question of specific causation. *Id.* at 276:12-16. Because he admits that neither he nor anyone else can offer an opinion that meets the standard of proof for specific

causation, his testimony will not "help the trier of fact" to decide the fundamental issue in this case. Fed. R. Evid. 702. It must therefore be excluded.

B. Dr. Handshoe Tried to Take Back His Admissions on But-For Causation

One day after Dr. Handshoe said there was "no way to know" which of 100 women with identical medical history to Ms. Daniels would develop diabetes due to Lipitor, *id.* at 260:10-22, he gave the opposite opinion as to Ms. Hempstead, which he termed "pure speculation."

> Q. So my question then is, which I think is a fair question, if you had 100 people just like Ms. Hempstead who took Lipitor the same and developed diabetes the same, would you say that all of them developed statin induced diabetes?
>
> A. Well, this is again, that hypothetical and if you want me to speculate, it's called pure speculation. ***I would say all 100 percent***. All – every Ms. Hempstead, if this is all Ms. Hempstead, exactly like Ms. Hempstead, all 100 will develop statin induced diabetes.

Handshoe *Hempstead* Tr. (Ex. 41) at 240:1-11.

The *Haller* court excluded similar expert evidence that was a "veritable moving target" whose "underpinnings … have changed in direct response" to litigation scrutiny. 598 F. Supp. 2d at 1296-97; *see also Miller v. Pfizer, Inc.*, 356 F.3d 1326, 1330 (10th Cir. 2004); *Glastetter v. Novartis Pharms. Corp.*, 107 F. Supp. 2d 1015, 1032 (E.D. Mo. 2000), *aff'd*, 252 F.3d 986 (8th Cir. 2001). In *Bausch & Lomb*, Judge Norton also rejected expert testimony that was "in flux throughout [the] litigation." *In re Bausch & Lomb, Inc. Contact Lens Solution Prods. Liab. Litig.*, 2009 WL 2750462, at *12 (D.S.C. Aug. 26, 2009). An expert's "willingness to abandon or qualify her opinions when faced with further facts, undermines the reliability of her opinions." *Id.* at *13. Dr. Handshoe's overnight reversal on the fundamental predicate of his report shows either that he has no reliable method and is making things up as he goes, or says whatever is needed to get to a pre-ordained result. Either way, it is anti-science and it is inadmissible.

IV. DR. HANDSHOE DEVIATES FROM HIS OWN PRACTICES OF PERSONAL EXAMINATION

To be reliable, a differential diagnosis or differential etiology "typically, though not invariably, 'is performed after physical examinations, the taking of medical histories, and the review of clinical tests, including laboratory tests.'" *Cooper*, 259 F.3d at 200 (quotation

omitted). Here, despite ready access to them as Plaintiffs' specific causation expert, Dr. Handshoe never examined or spoke with either Plaintiff. Handshoe *Daniels* Tr. (Ex. 6) at 39:18-25; Handshoe *Hempstead* Tr. (Ex. 41) at 20:15-21:5. Thus, none of Dr. Handshoe's conclusions are based on firsthand knowledge of the two Plaintiffs' conditions. Handshoe *Daniels* Tr. (Ex. 6) at 40:9-12; Handshoe *Hempstead* Tr. (Ex. 41) at 21:10-13. This situation deviates from his own typical practice whereby he seeks firsthand knowledge by examining and interviewing patients. Handshoe *Hempstead* Tr. (Ex. 41) at 21:25-22:22. Here, he arrived at his opinions on specific causation without any patient interaction. *Id.* at 22:23-23:4; Handshoe *Daniels* Tr. (Ex. 6) at 40:1-12. Dr. Handshoe admits that neither of Ms. Hempstead's treating physicians diagnosed her diabetes as statin-induced, but claimed that he is somehow better qualified to make this determination. Handshoe *Hempstead* Tr. (Ex. 41) at 81:11-23.

Dr. Handshoe's unjustified deviation in these cases from his own clinical practice of examining patients underscores the inadmissibility of his opinion. As the Fourth Circuit explained in *Cooper*, "*Kumho Tire* emphasizes that the purpose of Rule 702's gatekeeping function is to 'make certain that an expert ... employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.'" 259 F.3d at 203 (quoting *Kumho*, 526 U.S. at 152). Here, as in *Cooper*, Dr. Handshoe "had access to [the Plaintiffs], and yet, for purposes of this litigation, chose to deviate from his traditional method of evaluation," and his failure to "employ in the courtroom the same methods that he employs in his own practice" further illustrates the unreliability and inadmissibility of his opinion. *Id.*; *accord Haller*, 598 F. Supp. 2d at 1294-95; *Guinn*, 602 F.3d at 1251. Dr. Handshoe's *ipse dixit* that he is better qualified to evaluate causation than Plaintiffs' own physicians, despite his lack of examination and his lack of expertise concerning diabetes, is not to be credited.

V. DR. HANDSHOE MISAPPLIES THE BRADFORD HILL CRITERIA

In his reports, Dr. Handshoe purports to support his specific causation opinions by applying "the Bradford Hill criteria." Handshoe *Daniels* Rpt. (Ex. 45) at 11-13. Handshoe *Hempstead* Rpt. (Ex. 39) at 11-13. Yet the unreliability of Dr. Handshoe's opinion is further

evident in his misunderstanding and misapplication of the Bradford Hill factors, which are used to assess general – not specific – causation.

The Bradford Hill factors are applied only if multiple studies establish a statistically significant true association between an agent and a disease in order to evaluate "whether [the] observed association between a chemical and a disease is causal (*i.e.*, general causation)." *Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F. Supp. 2d 584, 592 (D.N.J. 2002); *see also Frischhertz v. SmithKline Beecham Corp.*, 2012 WL 6697124, at *3 (E.D. La. Dec. 21, 2012); *Dunn v. Sandoz Pharm. Corp.*, 275 F. Supp. 2d 672, 678-80 (M.D.N.C. 2003). These eight factors include "strength of relationship, consistency, specificity, temporality, dose response, biologic plausibility, coherence, experimental evidence, and analogy." *Dunn*, 275 F. Supp. 2d at 677 n.5. "[T]he Bradford Hill criteria are used to establish general causation from epidemiological studies – they are not used to establish specific causation." *In re Viagra Prods. Liab. Litig.*, 658 F. Supp. 2d 950, 958 (D. Minn. 2009); *accord Mallozzi v. EcoSMART Techs., Inc.*, 2013 WL 2415677, at *8 n.5 (E.D.N.Y. May 31, 2013).

All of this was lost on Dr. Handshoe. When questioned about what he understood of the Bradford Hill criteria, he offered a rambling explanation that conflated the criteria with differential diagnosis and described them as "legal driven" and "sort of a differential diagnostic method," evincing both his agenda for the criteria and his complete lack of understanding of their purpose. Handshoe *Hempstead* Tr. (Ex. 41) at 225:2-22.

Dr. Handshoe then explained that he applies the Bradford Hill criteria mentally as "a differential diagnosis on every person that [he] see[s]," which he explained is the "[s]ame methodology" as Bradford Hill. *Id.* at 226:3-7, 227:1-10. Yet after explaining that he applies the criteria (as a differential diagnosis) to everyone he sees, he confessed that the first time he ever read the Bradford Hill article was in this litigation. *Id.* at 227:11-22. Ultimately, Dr. Handshoe acknowledged that his use of Bradford Hill's general causation criteria for a specific causation assessment was contrary to his clinical practice and that he included it "[b]ecause that is the way that lawyers like reports to be structured and that's the way I structured my report." *Id.* at

227:23-228:2. "Well, lawyerly people like Bradford Hill criteria, so I was an expert in this case and I obliged them by doing the Bradford Hill criteria." *Id.* at 228:22-229:5.

Much like Dr. Handshoe's statement that the more than hundredfold difference between the risk attributable to weight gain and the alleged risk from statins makes them "roughly equivalent," his opinions regarding the Bradford Hill criteria are not simply unreliable, they are objectively wrong. The Bradford Hill factors for general causation are not in any way the "same methodology" as a differential diagnosis. The Bradford Hill factors are used to evaluate whether a true association observed in population-based studies is causal. A differential diagnosis is a tool used to evaluate potential causes of an individual patient's disease. Dr. Handshoe's complete misunderstanding of the criteria both evince his lack of qualification to evaluate specific causation here, as well the fact that his analysis is "legal driven [rather] than medicine driven," and conducted to oblige "lawyerly people." This unscientific opinion must be excluded.

CONCLUSION

For the foregoing reasons, Pfizer respectfully requests that this Court grant its motion and exclude the opinions of Plaintiffs' expert David K. Handshoe, M.D.

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CERTIFICATE OF SERVICE

I hereby certify that, this 7th day of August, 2015, I have electronically filed a copy of the above and foregoing with Clerk of the Court using the ECF system, which sent notification of such filing to counsel of record.

/s/ Mark S. Cheffo